Novel Five/Five- and Six/Five-Membered Bicyclic Nitroso Acetals from High-Pressure-Promoted Cyclisation Reactions of *p*-Methoxybenzyl Vinyl Ether, 1-Nitro-2-heteroaryl Ethenes, and Mono- and Di-Substituted Olefins

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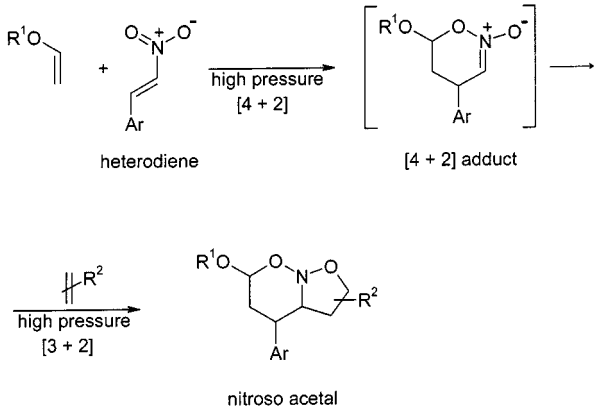
At 15 kbar the 1-nitro-2-heteroarylethenes **2a–c** reacted in a one-pot three-component cycloaddition with *p*-methoxybenzyl vinyl ether **(1)** and methyl acrylate to yield novel heteroaromatic-substituted six/five-membered bicyclic nitroso acetals. In the reaction of 3-[(*E*)-2-nitroeth-1-enyl]pyridine (2 equiv.) and **1** a competition between the formation of the tandem [4 + 2]/[3 + 2] cycloadducts and the formation of a novel five-membered cyclic nitronate was observed. The ratio of product formation was strongly pressure and solvent dependent. A mechanistic explanation for the formation of the novel five-membered cyclic nitronate has been proposed. 1-Nitro-4-[(*E*)-2-nitroeth-1-enyl]benzene **(2d)** reacted with **1** in the same manner as **2a** in accordance with the proposed mechanism. The five-membered cyclic nitronate reacted as an 1,3-dipole in a high-pressure promoted [3 + 2] cycloaddition with both electron-rich and electron-poor olefins and yielded a novel class of pyridyl-substituted five/five-membered bicyclic nitroso acetals.

Introduction

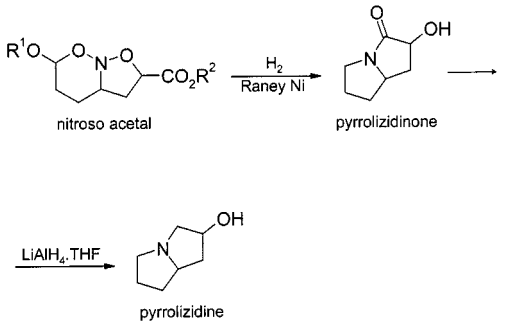
It has recently been shown that intermolecular tandem [4 + 2]/[3 + 2] cycloadditions between enol ethers, 1-nitro-2-arylethenes, and acrylates in the formation of six/five-membered bicyclic nitroso acetals are strongly promoted by the use of high-pressure.[1] High-pressure not only eliminates the need for Lewis acid catalysts[2] and excess of reagents,[3] but also allows the use of less reactive building blocks (e.g. di- and tri-substituted olefins and unactivated nitroalkenes).[4,5] In this tandem [4 + 2]/[3 + 2] cycloaddition, an electron-rich enol ether reacts with an electron-poor nitroalkene, which acts as a heterodiene, in an inverse electron demand Diels–Alder reaction to form the nitronate ([4 + 2] adduct) as shown in Scheme 1.



Scheme 1

The six-membered cyclic nitronate is a 1,3-dipole and can undergo a cyclisation reaction in the presence of an electron-poor or electron-rich alkene. Since there is a preference for the nitronate to react with electron-poor alkenes it is possible to perform this tandem [4 + 2]/[3 + 2] cycloaddition in a one-pot three component reaction with an electron-rich enol ether, a nitroalkene and an electron-poor alkene as dipolarophile. Furthermore, it has been shown that this high-pressure promoted multicomponent reaction is applicable to the solid phase with the use of either resin-bound acrylates or resin-bound nitroalkenes to obtain resin-bound nitroso acetals which can then be cleaved from the resin.[4,6]

Following development of this tandem [4 + 2]/[3 + 2] cycloaddition in the synthesis of heteroaromatic-substituted nitroso acetals, the behaviour of the 3′-pyridyl-, 3′-indolyl-, and 2′-pyrrolyl-substituted β-nitroethenes **2a–c** was studied (Scheme 3). Nitroso acetals have already been shown to be valuable precursors in the synthesis of the pyrrolizidinone and pyrrolizidine skeletons, therefore heteroaromatic-substituted nitroso acetals could be used as precursors in the synthesis of novel heteroaromatic-substituted pyrrolizidinones and pyrrolizidines (Scheme 2).[7,8]



Scheme 2

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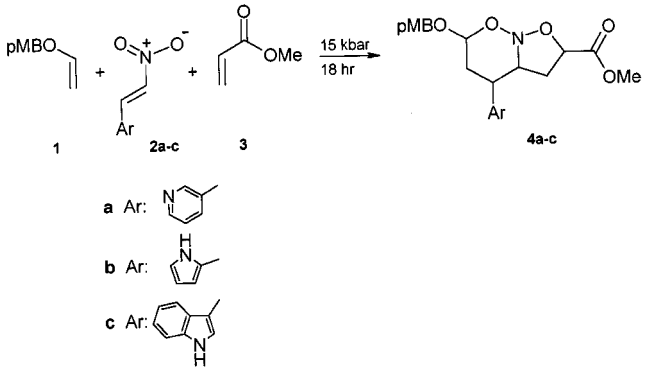
The alkaloid classes of pyrrolizidines, which are obtained after reduction of the corresponding pyrrolizidinones, have interesting biological properties. Some pyrrolizidinones have shown amnesia-reversal activity (Alzheimer's-related disease) while several pyrrolizidines have shown viral and retroviral suppression characteristics (including against HIV) as well as glycosidase inhibitory properties.[9,10] Furthermore it has been reported that pyrrolizidines play a role in the host-plant recognition process as pheromones.[11]

Results and Discussion

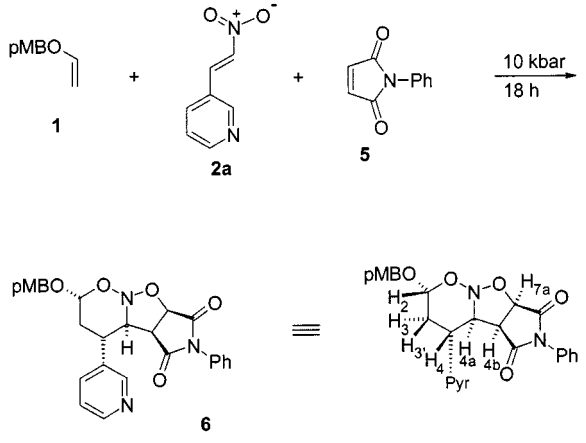
One-Pot Three-Component Reaction

At 15 kbar the β-nitroethenes **2a**, **2b**, and **2c** substituted with 3′-pyridyl-, 2′-pyrrolyl-, and 3′-indolyl, respectively, reacted efficiently with vinyl ether **1** and methyl acrylate **3** by means of the tandem [4 + 2]/[3 + 2] cycloaddition to form the six/five-membered bicyclic nitroso acetals **4** (Scheme 3).



Scheme 3

Compounds **4a**, **4b**, and **4c** were each obtained as mixtures of three diastereomers in 53−74% yield. The main diastereomers were obtained from a completely *endo*-selective [4 + 2] cycloaddition and an *exo*,*anti*-selective [3 + 2] cycloaddition (*anti* with respect to the aryl-group).[12] When *N*-phenyl maleimide **(5)** was used as the dipolarophile in the one-pot three-component reaction of **1** and **2a**, the resulting nitroso acetal **6** was obtained in 90% yield as one single diastereomer. This diastereomer arose from a completely

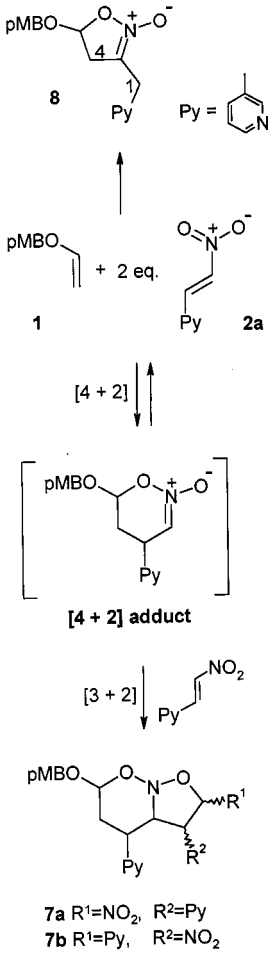


Scheme 4

endo-selective [4 + 2] and a completely *endo*-selective [3 + 2] cycloaddition after an *anti* approach with respect to the pyridyl group.[13] The stereochemistry was established with 2D-NOESY ^{1}H NMR showing NOE contacts between H_2, $H_{3'}$, and H_4, as well as between H_{4a}, H_{4b}, and H_{7a} (Scheme 4).

Unexpected Formation of *a Five*-Membered Cyclic Nitronate

In the reaction of 3-[(*E*)-2-nitroeth-1-enyl]pyridine **(2a)** (2 equiv.) and vinyl ether **1** an unexpected result was observed. At 15 kbar, nitroalkene **2a** yielded the tandem adducts in accordance with the sequence presented in Scheme 1. Nitroalkene **2a** reacted as a heterodiene with **1** and the excess of **2a** reacted as a dipolarophile with the in situ generated [4 + 2] adduct yielding nitroso acetals **7** in a one-pot reaction (Scheme 5).[14]



Scheme 5

However at lower pressures (as described below), the formation of a stable mono-adduct **8** was observed. Its formation appeared to be in competition with the formation of the bicyclic nitroso acetals **7a** and **7b**. Compound **8** was isolated by chromatographic purification, which allowed structural analysis. The proposed structure of the mono-adduct **8** (Scheme 5) was confirmed by mass spectroscopy, ^{13}C-Dept (3 × CH_2), ^{13}C-^{1}H correlation NMR and 2D-

NOESY ^{1}H NMR experiments (showing strong H_1-H_4 contacts).

Pressure and Solvent Dependency

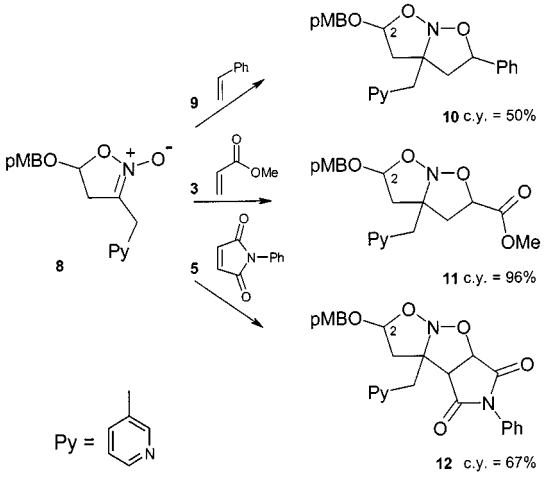
A clear pressure-dependent product ratio was observed in chloroform as solvent, Table 1. The ratio **7:8** (mono-adduct **8**/nitroso acetals **7a−b**) changed from 1:1 at 7 kbar to 3:1 at 12 kbar and 6:1 at 15 kbar.[15] In dichloromethane the **7:8** ratio was not influenced by the pressure (1:1 from 7−12 kbar).[16] An inverse product ratio (**7:8** = 1:8) was obtained when acetone was used as solvent — the mono-adduct **8** was now formed predominantly. An attempt to increase this ratio by application of a pressure of 15 kbar merely resulted in nitroalkene polymerisation. At pressures below 8 kbar conversion of starting compounds was not complete although the mono-adduct **8** was always formed as the main product.[17] A similar product ratio, although less pronounced, was obtained when tetrahydrofuran was used as the solvent (at 8 kbar, **7:8** = 1:4). Clearly both the pressure and the solvent play a crucial role in the formation of the five-membered cyclic nitronate **8**.

Table 1. Pressure and solvent dependent product ratio

Entry	Solvent	Pressure (kbar)	Ratio **7/8**
a	CH_2Cl_2	7−12	1:1
b	CH_2Cl_2	15	−
c	$CHCl_3$	7	1:1
d	$CHCl_3$	12	3:1
e	$CHCl_3$	15	6:1
f	acetone	15	−
g	acetone	8	1:8
h	THF	8	1:4

Novel *Five/Five*-Membered Bicyclic Nitroso Acetals

The mono-adduct **8** was reacted with several dipolarophiles (Scheme 6) to obtain additional chemical evidence for its structure. After a high-pressure-promoted 1,3-dipolar cycloaddition, the formation of the novel five/five-membered bicyclic nitroso acetals **10**, **11**, and **12** was achieved.[18] The cycloaddition with the mono-substituted dipolarophiles **9** and **3** proceeded with complete regioselectivity.



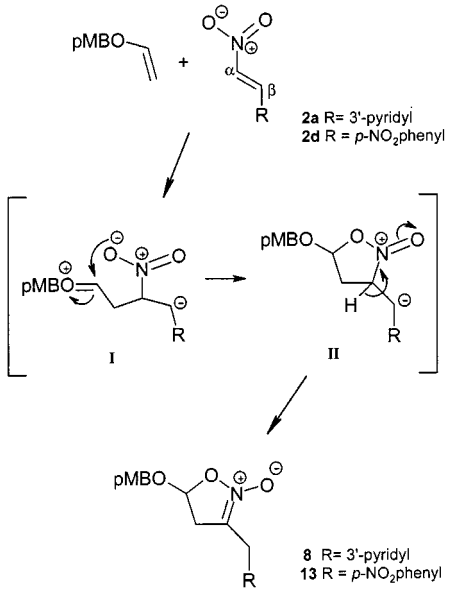
Scheme 6

The diastereomeric ratios of **10** (1:12:2), **11** (2:7:1), and **12** (12:2:15:3) were determined by ^{1}H NMR analysis of the crude reaction mixtures. For these compounds the major diastereomer was assigned on the basis of an *exo*,*anti* approach of the dipolarophile to the C(2) alkoxy substituent. The *anti*,*exo*-selectivity in the [3 + 2] cycloaddition is high for the mono-substituted alkenes **9** and **3** and low in the reaction with the disubstituted dipolarophile **5**.[19]

It is also noteworthy that the reaction of the 2′-pyrrolyl-**(2b)** and 3′-indolyl-substituted **(2c)** β-nitroethenes with enol ether **1** (at 8 kbar in acetone) did not result in the formation of a five-membered cyclic nitronate. In both cases the starting compounds were recovered.

Mechanistic Explanation

In an attempt to explain the formation of mono-adduct **8** the competing electron stabilising properties of the 3′-pyridyl group and the nitro group have to be considered. The anionic intermediate formed after a Michael-type addition of the enol ether to the α-nitro-carbon is stabilised by the 3′-pyridyl substituent, whereas addition to the β-nitro carbon results in formation of an anion stabilised by the nitro substituent.[20] The dipolar intermediate **I** is formed after attack of the enol ether at the α-position.[21] Ring closure of **I** gives the intermediate **II** and after a 1,2 proton-shift the five-membered mono-adduct **8** is formed (Scheme 7).



Scheme 7

To support this mechanism the reaction of 1-nitro-4-[(*E*)-2-nitroeth-1-enyl]benzene **(2d)** with **1** was investigated. Since the electronic inductive effect of the 3′-pyridyl group can be compared with that of a 4-nitrophenyl group,[22] nitroalkene **2d** was expected to react with enol ether **1** by a similar mechanism to form the five-membered cyclic nitronate **13**. Indeed, at 8 kbar the reaction afforded compound **13** as the only product as presented in Scheme 7.[23] The

formation of bicyclic nitroso acetals like **7** in which the excess of nitroalkene reacted as dipolarophile was not observed.

Since electron-donating substituents (e.g. 3′-indolyl- and 2′-pyrrolyl- and *p*-methoxyphenyl-substituted β-nitroethenes) do not stabilise the negative charge at the β-position they will not favour the formation of the five-membered cyclic nitronate. Owing to the unreactivity of these nitroethenes towards enol ether **1** at 8 kbar (in acetone) it was not possible to determine the effect of the heteroaromatic substituents on the **7/8** product ratio.

A summary of the findings is depicted in Scheme 5. The change in the **7/8** ratio from 1:1 at 7 kbar to 6:1 at 15 kbar in chloroform (Table 1, entry c−e) may suggest that at 15 kbar formation of the [4 + 2] adduct and the subsequent [3 + 2] cycloaddition with **2a** is faster than the formation of **8**.

However, at 8 kbar in acetone, formation of the tandem [4 + 2]/[3 + 2] adduct **7** seems much slower than the formation of **8**, as indicated by the **7/8** ratio of 1:8. Accumulation of **8** at lower pressures may suggest that **8** is the thermodynamic product while the [4 + 2] adduct is the kinetic product, which is in equilibrium with the starting compounds **1** and **2a**. Then it can be concluded that at lower pressure the [3 + 2] cycloaddition of **2a** with the [4 + 2] adduct is slower than the formation of **8**. Isolation of the intermediate [4 + 2] adduct would prove that the five-membered nitronate **8** can be formed from the six-membered [4 + 2] adduct under high-pressure conditions.[24] Unfortunately it was not possible to isolate the [4 + 2] adduct from the reaction mixture owing to its reactivity and low concentration. However, nitronate **8** appeared stable when kept for 24 hours at 15 kbar, which shows that **8** is formed irreversibly. The formation of the [3 + 2] cycloadduct of **8** and nitroalkene **2a** has not been observed at 8 kbar. This cycloaddition is expected to be much slower than the [3 + 2] cycloaddition of the [4 + 2] adduct with the nitroalkene **2a** due to the extra substituent on the C-atom of the dipole **8**.

The intriguing solvent and pressure effect is difficult to understand with the current data. Further investigations are required to obtain a satisfactory explanation for the effect of the solvent and pressure on the **7/8** ratio.[25]

Conclusion

The versatility of the high-pressure-promoted tandem [4 + 2]/[3 + 2] cycloaddition was demonstrated with the heteroaromatic-substituted nitroethenes **2a−c** in the formation of heteroaromatic-substituted nitroso acetals **7a−b**. By simple variation of the pressure it is now possible to generate the six/five-membered bicyclic nitroso acetals **4a−c** and the five/five-membered bicyclic nitroso acetals **10**, **11**, and **12** using 3-[(*E*)-2-nitro-1-ethenyl]pyridine as a building block. The six/five-membered bicyclic nitroso acetals **4a−c** can be prepared in a one-pot three-component reaction at 15 kbar and the novel five/five-membered bicyclic nitroso acetals **10**, **11**, and **12** can be prepared by means of a two-step procedure in which the five-membered cyclic nitronate **8** (formed at 8 kbar) is isolated prior to the [3 + 2] cycloaddition (at 10 kbar).

Experimental Section

General Remarks: Analytical thin layer chromatography was carried out on Merck glass-backed silica gel 60 F_{254} plates. − Column chromatography was carried out using Merck silica gel 60, 0.063−0.200 mm (70−230 mesh). − Infrared spectra were measured on a Bio-Rad FTS-25 single-beam spectrometer. − NMR spectra were measured on a Bruker AC-100, Bruker AC-300 or Bruker AM-400 with the indicated solvents, all with TMS as internal standard. *J* values are given in Hz. Products were purified by column chromatography using Merck silica gel 60. − Mass spectra were obtained with a double focusing VG7070E spectrometer or Varian Saturn GC/MS. − Elemental analyses were carried out on a Carlo Erba Instruments CHNSO EA 1108 element analyser. − Melting points were determined with a Reichert Thermopan microscope and are uncorrected. − The high-pressure apparatus operating at 1−15 kbar has been described before.[26]

1-Methoxy-4-[(vinyloxy)methyl]benzene (1): *p*-Methoxybenzyl alcohol (13.80 g, 0.10 mol) and *t*BuOK (5.60 g, 0.05 mol) were dissolved in dry THF (40 mL) in a glass tube. This red solution was cooled to −40 °C and acetylene gas (10 mL, 240 mmol) was bubbled through the solution. The glass tube was placed in an autoclave and the solution was stirred for 20 h at 120 °C at a pressure of 25 bar. The reaction mixture was distilled to yield **1** (14.89 g, 0.09 mmol, 91%) b.p. 71 °C, 0.1 Torr (ref.[27] b.p. 84 °C, 0.3 Torr). − ^{1}H NMR (100 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 4.06 (dd, ^{2+3}J = 2.1, 6.8, 2 H, H-2), 4.28 (dd, ^{2+3}J = 2.1, 14.6, 2 H, H-2′), 4.68 (s, 2 H, CH_2O), 6.55 (dd, ^{3+3}J = 6.8, 14.3, 1 H, H-1), 6.88 (d, $^3J_{ab}$ = 8.8, 2 H, Ph), 7.27 (d, $^3J_{ab}$ = 8.8, 2 H, Ph).

General Procedure 1: Microwave-Assisted Nitroalkene Synthesis: A mixture of arylaldehyde, CH_3NO_2 (5 equiv.) and NH_4OAc (1 equiv.) was mechanically stirred and exposed to microwave irradiation for the reported time using a modified microwave oven (Milestone Lavis-1000 basic) equipped with a condenser operating at 1000 W. After conversion of the aryl-aldehyde exceeded 90% (determined by GC-analysis) the reaction was stopped.

3-[(*E*)-2-Nitroeth-1-enyl]pyridine (2a):[33] A mixture of pyridine-3′-carboxaldehyde (5.00 g, 0.05 mol), CH_3NO_2 (5.12 g, 0.08 mol), *t*BuOH (30 mL), and THF (30 mL) was stirred at 0 °C and *t*BuOK (310 mg, 0.06 equiv.) was added. After 2 h the conversion of the aldehyde was complete (monitored by TLC with EtOAc as eluent) and the mixture was diluted with H_2O (25 mL) and Et_2O (50 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (25 mL) and brine. The aqueous layer was back extracted with Et_2O (50 mL) . The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo to afford the β-nitro alcohol (7.44 g, 0.04 mol, 95%) as a yellow oil. − ^{1}H NMR (100 MHz, $CDCl_3$): δ = 4.57 (dd, ^3J = 4.7, 8.1, 2 H, H-2), 5.53 (dd, ^3J = 5.0, 7.9, 1 H, H-1), 7.35 (dd, ^3J = 4.9, 7.9, 1 H, pyrH-5), 7.84 (dt, ^{4+3}J = 1.9, 8.0, 1 H, pyrH-4), 8.43 (dd, ^{4+3}J = 1.6, 4.9, 1 H, pyrH-6), 8.51 (d, ^4J = 2.0, 1 H, pyrH-2).

β-Nitro alcohol (5.02 g, 0.03 mol), DMAP (180 mg, 2 mmol, 0.05 equiv.) and Ac_2O (3.34 g, 0.03 mol, 1.1 equiv.) were dissolved in CH_2Cl_2 (150 mL) and stirred for 2 h, after which time the solution was neutralised with saturated aqueous $NaHCO_3$ (50 mL). The organic layer was washed with brine and the aqueous layer was back extracted with 2 × 50 mL CH_2Cl_2. The combined organic layers

were dried with $MgSO_4$, filtered, and concentrated in vacuo to afford **2a** (2.91 g, 0.02 mol, 65%). − ^{1}H NMR (100 MHz, $CDCl_3$): δ = 7.42 (dd, ^3J = 4.8, 7.7, 1 H, PyH-5); 7.63 (d, ^3J = 13.8, 1 H, H-1), 7.88 (m, 1 H, PyH-4), 8.03 (d, ^3J = 13.8, 1 H, H-2), 8.73 (dd, ^{4+3}J = 1.6, 4.8, 1 H, pyrH-6), 8.80 (d, ^4J = 2.1, 1 H, pyrH-2). − M.p. 136−138 °C (ref.[28] 141 °C, cryst. from petroleum ether or EtOAc). The one-pot microwave synthesis (general method 1) of **2a** yielded only 20% conversion of the aldehyde whereas other literature procedures for the synthesis of **2a** failed.[28,29]

2-[(*E*)-2-Nitroeth-1-enyl]-1*H*-pyrrole (2b): Compound **2b** was prepared according to general procedure 1 with pyrrole-2′-carboxaldehyde (990 mg, 10 mmol), CH_3NO_2 (3.20 g, 0.05 mol) and NH_4OAc (810 mg, 11 mmol). After 10 min. reflux, the conversion was higher than 90%. Purification over a short silica column with EtOAc/hexane (1:1, *v*/*v*) as eluent afforded **2b** (1.01 g, 0.07 mol, 70%). − ^{1}H NMR (100 MHz, $CDCl_3$): δ = 6.39 (m, 1 H, pyrr-*H*), 6.75 (br. s, 1 H, pyrr-*H*), 7.12 (br. s, 1 H, pyrr-*H*), 7.50 (d, ^3J = 13.3, 1 H, H-1), 7.98 (d, ^3J = 13.3, 1 H, H-2). M.p. 98−103 °C (ref.[30] 103 °C, cryst. from EtOH).

3-[(*E*)-2-Nitroethenyl]-1*H*-indole (2c): Compound **2c** was prepared according to general procedure 1 with indole-3′-carboxaldehyde (1.00 g, 0.07 mol), CH_3NO_2 (2.10 g, 0.03 mol) and NH_4OAc (530 mg, 7 mmol). After 40 min. reflux, the conversion of the aldehyde was 95%. Purification over a short silica column using EtOAc/hexane (1:2 *v*/*v*) as eluent afforded **2c** (1.18 g, 0.06 mol, 91%) . − ^{1}H NMR (100 MHz, $CDCl_3$): δ = 7.7−7.3 (m, 5 H, ind-*H*), 7.8 (d, ^3J = 13.5, 1 H, H-1), 8.3 (d, ^3J = 13.5, 1 H, H-2). − M.p. 166−169 °C, (ref. 171−172 °C,[31] 165−167 °C,[32] cryst. from aq. ethanol or 95% EtOH).

1-Nitro-4-[(*E*)-2-nitroeth-1-enyl]benzene (2d):[33] A mixture of 4-nitro-benzaldehyde (1.00 g, 0.07 mol), CH_3NO_2 (730 mg, 12 mmol), *t*BuOH (6 mL), and THF (6 mL) was stirred at 0 °C and *t*BuOK (5 mg, 0.06 equiv.) was added. Within 2 h conversion of the aldehyde was complete. The mixture was diluted with H_2O (25 mL) and Et_2O (50 mL) and the organic layer was washed with saturated aqueous $NaHCO_3$ (25 mL) and brine. The aqueous layer was back extracted with Et_2O (50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo to afford the β-nitro alcohol (1.27 g, 0.06 mol, 91%). − ^{1}H NMR (100 MHz, $CDCl_3$): δ = 4.2 (br. s, 1 H, O*H*), 4.6 (m, 1 H, CH_2−NO_2), 4.5 (d, ^3J = 6.4, 1 H, CH_2NO_2), 5.5 [t, ^3J = 6.3, 1 H, C*H*(OH)], 7.5 (d, ^3J = 8.6, 2 H, Ar-*H*), 8.1 (d, ^3J = 8.6, 2 H, Ar-*H*).

β-Nitro alcohol (1.27 g, 0.06 mmol), DMAP (37 mg, 0.3 mmol, 0.05 equiv.) and Ac_2O (710 mg, 7 mol, 1.13 equiv.) were dissolved in CH_2Cl_2 (50 mL). After stirring for 2 h, a saturated solution of $NaHCO_3$ (25 mL) was added and the organic layer was washed with brine. The aqueous layer was back extracted with CH_2Cl_2 (25 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo to afford **2d** (950 g, 5 mmol, 82%). The compound shows poor solubility in most solvents (CH_2Cl_2, EtOAc and EtOH). In acetone slightly better solubility is observed. ^{1}H NMR (300 MHz, $CDCl_3$/MeOH): δ = 7.90 (d, ^3J = 8.8, 2 H, ArH-3,5), 7.96 (d, ^3J = 13.7, 1 H, H-1), 8.11 (d, ^3J = 13.7, 1 H, H-2), 8.29 (d, ^3J = 8.8, 2 H, ArH-2,6). − M.p. 170−172 °C (ref. 168−172 °C,[34] 173 °C[35]). General procedure 1 appeared to be unsuccessful; after 50 min. no conversion of the aldehyde was observed (GC-analysis).

General Procedure 2: High-Pressure-Promoted One-Pot, Three-Component Tandem [4 + 2]/[3 + 2] Cycloaddition: The prescribed amount of the nitroalkene, the enol ether (1 equiv.) and the dipolarophile (1.1 equiv.) were dissolved in CH_2Cl_2 (unless stated otherwise) in a 7.5 mL Teflon tube. The closed tube was placed at the prescribed pressure for 18 h. After depressurisation, the reaction mixture was concentrated in vacuo and the products were separated by column chromatography on silica 60 [EtOAc/hexane; 1% (*v*/*v*) Et_3N].

Methyl 6-[(4-Methoxybenzyl)oxy]-4-(3-pyridyl)perhydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylate (4a): Compound **4a** was prepared according to general procedure 2 with **2a** (174 mg, 1.2 mmol), **1** (168 mg, 1.0 mmol) and **3** (296 mg, 3.4 mmol). After chromatographic purification (EtOAc), **4a** (301 mg, 0.8 mmol, 74%) was obtained as a mixture of three diastereomers as a clear oil. A second chromatographic purification (EtOAc/hexane 3:1) and subsequent crystallisation from CH_2Cl_2/hexane yielded the major diastereomer as a white solid, m.p.: 109−110 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12−2.03 (m, 1 H, H-5′), 2.32−2.21 (m, 1 H, H-5), 2.58−2.48 (m, 2 H, H-3), 2.98−2.91 (m, 1 H, H-4), 3.75 (s, 3 H, OCH_3), 3.78 (m, 1 H, H-3a), 3.80 (s, 3 H, OCH_3), 4.58 (d, ^2J = 11.5, 1 H, H-1), 4.90 (d, ^2J = 11.5, 1 H, H-1′), 5.02 (t, ^3J = 6.9, 1 H, H-6), 5.16 (dd, ^3J = 4.2, 8.6, 1 H, H-2), 6.88 (m, ^3J = 8.6, 2 H, PhH-3,5), 7.33−7.26 (m, 3 H, PyH-4, PhH-2,6), 7.64 (m, 1 H, PyH-6), 8.52 (m, 2 H, PyH-2). − ^{13}C NMR (75 MHz, $CDCl_3$): δ(170.4, 160, 149.2, 148.9, 137.2, 134.9, 129.7, 123.9, 113.8, 98.4, 81.5, 74.7, 68.9, 55.3, 52.6, 41.0, 35.3, 32.6. − CI-MS: *m*/*z* (%) = 401 [MH^+] (31), 383 (9), 341 (27), 300 (10), 166 (27), 138 (64), 121 [*p*-methoxybenzyl cation] (100), 109 (45), 87 (26), 77 (25), 55 (43). − $C_{21}H_{24}N_2O_6$ (400): calcd. C 62.99, H 6.04, N 7.00; found C 62.55, H 6.14, N 6.93.

Methyl 6-[(4-Methoxybenzyl)oxy]-4-(1*H*-pyrrol-2-yl)perhydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylate (4b): Compound **4b** was prepared according to general procedure 2 with **2b** (300 mg, 2.2 mmol), **1** (180 mg, 1.1 mmol) and **3** (300 mg, 3.5 mmol) dissolved in $CHCl_3$/EtOAc = 1:10. After chromatographic purification (EtOAc/hexane 1:2) **4b** (230 mg, 0.7 mmol, 53%) was obtained as a mixture of three diastereomers and **1** (30 mg, 0.2 mmol, 20%) was recovered. A second chromatographic purification and subsequent crystallisation from CH_2Cl_2/hexane yielded the major diastereomer as white needles, m.p.: 131−134 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98−1.90 (m, 1 H, H-5′), 2.25−2.14 (m, 1 H, H-5), 2.51−2.46 (m, 1 H, H-3′), 2.60 (dd, ^{3+2}J = 1.5, 10.5, 1 H, H-3), 3.32−3.26 (m, 1 H, H-4), 3.69 (m, 1 H, H-3a), 3.73 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 4.55 (d, ^2J = 11.1, 1 H, H-1′), 4.96 (d, ^2J = 11.1, 1 H, H-1), 5.09−5.04 (m, 2 H, H-2), 5.91 (m, 1 H, pyrH-4), 6.02 (m, 1 H, pyrH-3), 6.53 (m, 1 H, pyrH-5), 6.88 (m, ^3J = 8.6, 2 H, PhH-3,5), 7.32 (m, ^3J = 8.6, 2 H, PhH-2,6), 9.32 (br. s, 1 H, N*H*). − CI-MS: *m*/*z* (%) = 389 [MH^+] (2), 268 (2), 237 (14), 235 (5), 147 (23), 138 (8), 122 (37), 121 [100] (*p*-methoxybenzyl cation), 94 (12). − $C_{20}H_{24}N_2O_6$ (388): calcd. C 61.85, H 6.23, N 7.21; found C 62.13, H 6.13, N 7.20.

Methyl 4-(1*H*-Indol-3-yl)-6-[(4-methoxybenzyl)oxy]perhydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylate (4c): Compound **4c** was prepared according to general procedure 2 with **2c** (300 mg, 1.7 mmol), **1** (260 mg, 1.6 mmol) and **3** (170 mg, 2.0 mmol) in acetone (dried over 4 Å mol. sieves; poor solubility of **2c** in chloroform). ^{1}H NMR analysis of the crude reaction mixture showed 80% conversion of the enol ether. After chromatographic purification (EtOAc/hexane 1:1) **4c** (410 mg, 0.5 mmol, 59%) was obtained as a mixture of three diastereomers. A second chromatographic purification yielded the minor diastereomer as a clear oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19−2.12 (m, 1 H, H-5′), 2.46−2.36 (dt, ^{3+2}J = 7.8, 13.5, 1 H, H-5), 2.70 (t, ^3J = 8.4, 2 H, H-3), 3.32−3.23 (m, 1 H, H-4), 3.80 (s, 3 H, OCH_3), 3.82 (m, 1 H, H-3a), 3.86 (s, 3 H, OCH_3), 4.61 (d, ^2J = 11.7, 1 H, H-1′), 4.80 (t, ^3J = 8.0, 1 H,

H-2), 4.92 (d, ^2J = 11.7, 1 H, H-1), 5.04 (t, ^3J = 7.2, 1 H, H-6), 6.87 (d, ^3J = 8.6, 2 H, PhH-3,5), 7.40−7.06 (m, Ind-*H*, 3 H, PhH-3,5), 7.64 (d, ^3J = 7.8, 1 H, Ind-*H*), 8.10 (br. s, 1 H, N*H*). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4, 160, 136.4, 129.9, 126.0, 122.4, 121.1, 119.8, 119.7, 116.4, 113.8, 111.3, 98.9, 81.5, 75.0, 71.3, 55.2, 52.6, 36.2, 36.2, 32.7. − CI-MS: *m/z* (%) = 439 [MH^+] (1), 438 (1), 303 (14), 302 (10), 271 (8), 237 (8), 225 (6), 199 (12), 198 (11), 172 (23), 171 (21), 170 (12), 169 (8), 144 (15), 143 (48), 139 (14), 138 (35), 137 (26), 130 (17), 122 (22), 121 [*p*-methoxybenzyl cation] (100), 117 (21), 109 (30), 107 (12), 91 (11), 78 (10), 77 (18), 70 (20), 55 (20). − HRMS calcd. for $C_{21}H_{24}N_2O_6$: 438.17909; found 438.17955 ± 0.00058.

Hexahydro-2-[(4-methoxybenzyl)oxy]-6-phenyl-4-(3-pyridyl)pyrrolo[3′,4′:4,5]isoxazolo[2,3-*b*][1,2]oxazine-5,7-dione (6): Compound **6** was prepared according to general procedure 2 with **2a** (20 mg, 0.1 mmol), **1** (22 mg, 0.1 mmol) and *N*-phenyl maleimide (**5**; 25 mg, 0.1 mmol). After column chromatography (EtOAc/hexane 3:1) **6** (60 mg, 0.1 mmol, 90%) was obtained as a single stereoisomer. White solid (from CH_2Cl_2/hexane) m.p.: 175−178 °C. − ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.07−1.99 (m, 1 H, H-3′), 2.38−2.25 (dt, ^{3+2}J = 7.9, 13.6, 1 H, H-3), 3.74−3.68 (m, 2 H, H-4, H-4b), 3.76 (s, 3 H, OCH_3), 3.92 (dd, ^3J = 7.0, 8.9, 1 H, H-4a), 4.59 (d, ^2J = 11.7, 1 H, H-1′), 4.83 (d, ^2J = 11.7, 1 H, H-1), 4.90 (t, ^3J = 6.7, 1 H, H-2), 5.28 (d, ^3J = 8.0, 1 H, H-7a), 6.96 (m, ^3J = 8.6, 2 H, PhH-3,5), 7.52−7.19 (m, 8 H, Py-H6 and N-Ph, PhH-2,6), 7.75 (d (br), ^3J = 8.1, 1 H, Py-H5), 8.53 (m, 1 H, Py-H4), 8.70 (br. s, 1 H, Py-H2). − CI-MS: *m/z* (%) = 488 [MH^+] (1.1), 457 (0.6), 435 (0.8), 350(0.9), 315 (6.2), 291 (2.7), 268 (2.3), 240 (2.7), 174 (30.5), 173 (55), 138 (37.1), 121 [*p*-methoxybenzyl cation] (100), 109 (24), 91 (20), 77 (24), 51 (17). − $C_{27}H_{25}N_3O_6$ (487): calcd. C 66.52, H 5.17, N 8.62; found C 66.27, H 5.26, N 8.45.

4,5-Dihydro-5-[(4-methoxybenzyl)oxy]-3-(3-pyridylmethyl)isoxazolium-2-olate (8): Compound **2a** (900 mg, 6.0 mmol) and **1** (270 mg, 1.7 mmol) were dissolved in acetone in a 7.5 mL Teflon tube and placed at 8 kbar. An excess of **2a** was used since the compound slowly polymerises under high-pressure conditions. After 18 h the pressure was released and chromatographic purification (EtOAc) afforded **8** (240 mg, 0.8 mmol, 44%) as a clear oil. − ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.11 (m, 1 H, H-4′), 2.26 (m, 1 H, H-4), 2.76 (m, 1 H, H-1′), 3.05 (m, 1 H, H-1), 3.80 (3 H, s, O*CH*$_3$), 4.70 (d, ^2J = 11.4, 1 H, H-1′), 4.95 (d, ^2J = 11.4, 1 H, H-1), 5.51 (dd, ^3J = 2.7, 4.1, 1 H, H-5), 6.88 (m, ^3J = 8.6, 2 H, PhH-3,5), 7.19 (m, ^3J = 8.6, 2 H, PhH-2,6), 7.37 (m, 1 H, PyH-5), 8.57 (ddd, $^{4+4+3}J$ = 1.6, 1.9, 9.0, 2 H, PyH-4,6), 9.05 (d, ^4J = 1.9, 1 H, PyH-2). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5, 149.5, 147.9, 134.8, 129.9, 128.3, 128.0, 123.0, 119.8, 113.9, 100.6, 70.0, 55.2, 24.9, 20.9. − CI-MS: *m/z* (%) = 315 [MH^+] (44), 299 (31), 284 (22), 255 (13), 240 (22), 205 (27), 179 (18), 138 (44), 121 [*p*-methoxybenzyl cation] (100) (109 (30), 78 (16), 51 (13). − HRMS calcd. for $C_{17}H_{18}N_2O_4$: 314.12666; found 314.12633 ± 0.00063.

Determination of Solvent and Pressure Dependency in the High-Pressure-Promoted Two-Component Tandem [4 + 2]/[3 + 2] Cycloaddition of 2a and 1: Nitroalkene **2a** (66 mg, 0.4 mmol, 4 equiv.) and enol ether **7** (16 mg, 0.1 mmol) were dissolved in the prescribed solvent in a 1.5 mL Teflon tube. The closed tube was placed at the prescribed pressure for 18 h. After depressurisation, the crude reaction mixtures were analysed by ^{1}H NMR (300 MHz, $CDCl_3$). Determination of product ratios **7**/**8** was achieved by integration of the signals of mono-adduct **8** (-OC*H*O-, 1 H) at δ = 5.5 and the set of signals between δ = 6.0 and 6.3 from regio-isomers **7** (***exo*-7b**- [δ = 6.0], ***endo*-7b** [δ = 6.2] and **7a** [δ = 6.3]), Figure 1. The assignments of compounds **7** were made based on previous analysis of the fully characterised regio-isomers found in the reaction of **1** with β-nitrostyrene described in ref.[5]

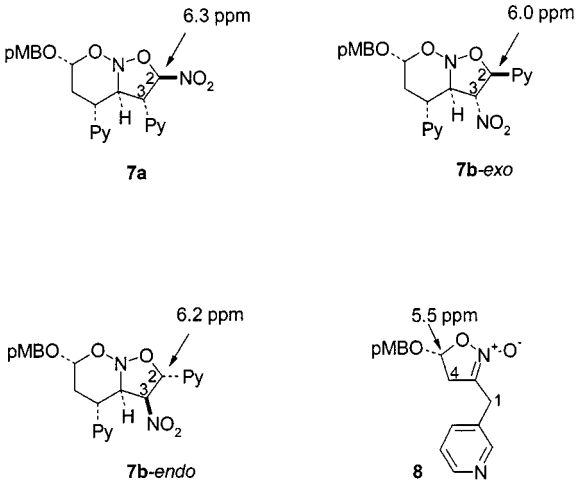


Figure 1. Specific NMR spectroscopic data of compound **8** and **7**

General Procedure 3: Synthesis of Five/Five-Membered Bicyclic Nitroso Acetals: The prescribed amount of mono-adduct **8** and alkene (1.5 equiv.) were dissolved in chloroform in a Teflon tube. The closed tube was placed at 10 kb for 18 h. After depressurisation, the reaction mixture was concentrated in vacuo and the products were separated by column chromatography on silica 60 (EtOAc/hexane; 1% (*v*/*v*) Et_3N).

2-[(4-Methoxybenzyl)oxy]-5-phenyl-3a-(3-pyridylmethyl)perhydroisoxazolo[2,3-*b*]isoxazole (10): Compound **10** was prepared according to general procedure 3 with **8** (30 mg, 0.1 mmol) and styrene **9** (22 mg, 0.2 mmol). A pressure of 10 kbar was applied for 36 h. After chromatographic purification (EtOAc/hexane 3:1), **10** (20 mg, 0.05 mmol, 50%) was obtained as a mixture of three diastereomers in a 12:2:1 ratio. A second chromatographic purification afforded the major diastereomer in pure form (clear oil). − ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.73 (m, 1 H, H-3′), 1.99 (m, 1 H, H-3), 2.14 (m, 1 H, Py-CH_2), 2.31(m, 1 H, Py-CH_2), 2.59 (dd, ^{3+2}J = 5.6, 12.3, 1 H, H-4), 3.81 (s, 3 H, OCH_3), 3.16 (dd, ^{3+2}J = 9.5, 12.3, 1 H, H-4′), 4.64 (d, ^2J = 11.4, 1 H, H-1′), 5.0 (d, ^2J = 11.4, 1 H, H-1), 5.12 (t, ^3J = 4.2, 1 H, H-2), 5.81 (dd, ^3J = 5.6, 9.5, 1 H, H-5), 6.90 (m, 2 H, PhH-3,5), 7.15 (m, 5 H, Ph), 7.26 (m, 1 H, PyH-5), 7.36 (m, PhH-3,5), 7.91 (m, 1 H, PyH-4), 8.50 (dd, ^{4+3}J = 1.6, 4.7, 1 H, PyH-6), 8.70 (d, ^4J = 2.3, 1 H, PyH-2). − CI-MS: *m/z* (%) = 419 [MH^+] (24), 283 (35), 267 (41), 225 (5), 162 (7), 161 (8), 121 [*p*-methoxybenzyl cation] (100). − HRMS calcd. for $C_{25}H_{26}N_2O_4$ [MH^+]: 419.19708; found 419.19717 ± 0.00096.

Methyl 5-[(4-Methoxybenzyl)oxy]-3a-(3-pyridylmethyl)perhydroisoxazolo[2,3-*b*]isoxazole-2-carboxylate (11): Compound **4a** was prepared according to general procedure 3 with **8** (118 mg, 0.4 mmol) and **3** (53 mg, 0.5 mmol). After chromatographic purification (EtOAc/hexane 4:1) **11** (146 mg, 0.4 mmol, 96%) was obtained as a mixture of three diastereomers in a 7:2:1 ratio. The major diastereomer (clear oil) was isolated after a second chromatographic purification. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.74 (m, 1 H, H-3), 1.95 (m, 1 H, H-3), 2.09 (m, 1 H, Py-CH_2), 2.35 (m, 1 H, Py-CH_2), 2.92 (dd, ^{3+2}J = 3.4, 12.6, 1 H, H-4), 3.09 (dd, ^{3+2}J = 10.3, 12.6, 1 H, H-4′), 3.48 (s, 3 H, O*CH*$_3$), 3.81 (s, 3 H, O*CH*$_3$), 4.60 (d, ^2J = 11.3, 1 H, H-1′), 4.98 (d, ^2J = 11.3, 1 H, H-1), 5.05 (t(br), ^3J = 4.2, 1 H, H-2), 5.16 (dd, ^3J = 3.4, 10.3, 1 H,

H-5), 6.90 (d, ^3J = 11.7, 2 H, PhH-3,5), 7.25 (m, 1 H, pyrH-5), 7.35 (d, ^3J = 11.7, 2 H, PhH-2,6), 7.88 (m, 1 H, pyrH-4), 8.49 (br. s, 1 H, pyrH-6), 8.68 (br. s, 1 H, pyrH-2). − CI-MS: *m/z* (%) = 401 [MH^+] (100), 299 (19), 265 (79), 249 (58), 207 (13), 163 (12), 138 (16), 122 (17). − HRMS calcd. for $C_{21}H_{25}N_2O_6$ [MH^+]: 401.17126; found 401.17080 ± 0.00060. − HRMS calcd. for $C_{21}H_{24}N_2O_6$ [M^+]: 400.16344; found 400.16318 ± 0.00036.

2-[(4-Methoxybenzyl)oxy]-5-phenyl-3a-(3-pyridylmethyl)perhydroxisoxazolo[2,3-*b*]pyrrolo[3,4-*d*]isoxazole-4,6-dione (12): Compound **12** was prepared according to general procedure 3 with **8** (38 mg, 0.1 mmol) and *N*-phenyl maleimide (**5**; 22 mg, 0.1 mmol). After chromatographic purification (EtOAc) two diastereomers **12a** and **12b** were obtained in 40% (23 mg, 0.05 mmol) and 27% (16 mg, 0.03 mmol) yield, respectively.

12a (white solid from CH_2Cl_2/hexane), m.p.: 155−159 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.80 (m, 1 H, H-3), 2.07 (m, 1 H, H-3), 2.63 (m, 2 H, Py-CH_2), 3.80 (s, 3 H, OCH_3), 4.22 (d, ^3J = 8.4, 1 H, H-3b), 4.63 (d, ^2J = 11.5, 1 H, H-1′), 4.92 (d, ^2J = 11.5, 1 H, H-1), 5.12 (t, ^3J = 3.8, 1 H, H-2), 5.61 (d, ^3J = 8.4, 1 H, H-6a), 6.55 (m, 2 H, Ph), 6.88 (m, ^3J = 8.5, 2 H, PhH-3,5), 7.49−7.23 (m, 6 H, pyrH-5, PhH-2,6, Ph), 7.91 (m, 1 H, pyrH-4), 8.57 (d, ^4J = 4.6, 1 H, pyrH-6), 8.80 (d, ^4J = 2.2, 1 H, pyrH-2). − CI-MS: *m/z* (%) = 488 (1), 457 (2), 435 (3), 315 (16), 314 (11), 240 (14), 179 (30), 174 (67), 173 (63), 161 (12), 149 (15), 138 (29), 137 (18), 122 (29), 121 [*p*-methoxybenzyl cation] (100), 109 (22), 91 (19), 77 (19), 57 (19), 51 (14). − $C_{27}H_{25}N_3O_6$ (488): calcd. C 66.52, H 5.17, N 8.62; found C 66.02′,H 4.92, N 8.44.

12b (clear oil)**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.88−1.76 (m, 2 H, H-3), 2.24−2.17 (m, 1 H, Py-CH_2), 2.87−2.80 (m, 1 H, Py-CH_2), 3.81 (s, 3 H, OCH_3), 3.97 (d, ^3J = 8.4, 1 H, H-3b), 4.60 (d, ^2J = 11.5, 1 H, H-1′), 4.97−4.90 (m, 2 H, H-2, H-1), 5.13 (d, ^3J = 8.4, 1 H, H-6a), 6.88 (m, ^3J = 8.6, 2 H, PhH-3,5), 7.50−7.21 (m, 8 H, pyrH-5, PhH-2,6, Ph), 7.90 (m, 1 H, pyrH-4), 8.57 (d, ^4J = 4.7, 1 H, pyrH-6), 8.82 (d, ^4J = 2.1, 1 H, pyrH-2).

4,5-Dihydro-5-[(4-methoxybenzyl)oxy]-3-(4-nitrobenzyl)isoxazol-2-ium-2-olate (13): Compound **13** (213 mg, 1.1 mmol) and **1** (90 mg, 0.6 mmol) were reacted in acetone at 8 kbar for 18 h. After depressurisation, column chromatography (EtOAc/heptane 1:1) afforded **13** (55 mg, 0.3 mmol, 46%) as a clear oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15−2.08 (m, 1 H, H-4′), 2.33−2.25 (m, 1 H, H-4), 2.81−2.71 (m, 1 H, Py-CH_2), 3.10−3.01 (m, 1 H, Py-CH_2), 3.79 (s, 3 H, OCH_3), 4.69 (d, ^2J = 11.4, 1 H, H-1′), 4.94 (d, ^2J = 11.4, 1 H, H-1), 5.53 (dd, ^3J = 2.7, 4.2, 1 H, H-5), 6.88 (d, ^3J = 8.6, 2 H, PhH-3,5), 7.28 (d, ^3J = 8.6, 2 H, PhH-2,6), 8.17 (d, ^3J = 7.1, 2 H, *p*NO_2PhH-3,5), 8.24 (d, ^3J = 7.1, 2 H, *p*NO_2PhH-2,6). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5, 147.1, 137.7, 129.9, 128.2, 120.9, 113.9, 113.8, 100.9, 70.1, 55.2, 25.2, 21.4. − CI-MS: *m/z* (%) = 359 [MH^+] (0.3), 343 (2), 313 (1), 224 (7), 223 (58), 207 (14), 193 (2), 178 (3), 177 (4), 175 (4), 159 (1), 138 (16), 121 (100, *p*-methoxybenzyl cation). − HRMS calcd. for $C_{18}H_{18}N_2O_6$ [MH^+]: 359.12431; found 359.12415 ± 0.00165.

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[13] The *anti*-attack of the bulky *N*-phenyl maleimide dipolarophile is probably due to the steric hindrance of the pyridyl- and *p*-methoxybenzyl-substituents which shield one side of the nitronate, whereas the *endo*-selectivity might arise from secondary orbital overlap between the *N*-phenyl-substituent and the nitronate dipole.

[14] For a detailed study of the reaction between vinyl ether **1** and β-nitrostyrene and subsequent β-lactam formation, see ref. [5].

[15] The **7/8** ratio was extracted from ^{1}H NMR analysis of the crude reaction mixtures and integration of the corresponding proton signals; see Experimental Section.

[16] Increasing the pressure from 12 to 15 kbar merely resulted in polymerisation of the starting compound **2a**.

[17] The conversion of **1** was measured by ^{1}H NMR analysis of the crude reaction mixtures; 95% at 8 kbar, 50% at 6 kbar and 20% at 4 kbar.

[18] The reaction of nitronates as dipoles in [3 + 2] cycloadditions was first discovered by: V.A. Tartakovskii, I. E. Chlenov, S. S. Smagin, S. S. Noviov, *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1964**, 583−584; V. A. Tartakovskii, *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1984**, *1*, 165−173; also described by K. B. G. Torssell, in: *Nitrile oxides, Nitrones and Nitronates in Organic Synthesis* (Ed. H. Feuer), VCH Publishers, Inc., New York, **1988**.

[19] Assignment was based on 2D-NOESY NMR studies of the main diastereomers of **10** (80%), **11** (70%) and **12** (47%). The diastereomer of compound **11** formed in 30% and the diastereomer of compound **12** formed in 40% yield have been assigned on the basis of an *endo,anti* approach to the C(2) alkoxy substituent.

[20] α-Nitro attack results in formation of a six-membered cyclic nitronate and β-nitro attack results in formation of the five-membered cyclic nitronate.

[21] High-pressure typically stabilises and promotes the formation of charged intermediates as described, in: *Organic Synthesis At High-pressures* (Eds.: K. Matsumoto, R. Morrin Acheson, John Wiley & Sons, Inc., **1991**.

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[23] ^{1}H NMR analysis of the crude reaction mixture showed 75% conversion of enol ether **1**.

[24] The reversibility of the Diels−Alder reaction under high-pressure conditions has been described in the literature. See for example: F-G. Klärner, V. Breitkopf, *Eur. J. Org. Chem.* **1999**, 2757−2762 and references therein.

[25] At the moment we have not found a satisfactory explanation for the observed solvent and pressure effects. There seems to be no correlation between the dielectric constant of the solvents (CH_2Cl_2 8.93; $CHCl_3$ 4.81; THF 7.58; acetone 20.56) or the difference in freezing pressure of the solvent (CH_2Cl_2, THF, and acetone >20 kbar; $CHCl_3$, 5.5 kbar) and the change in the **7/8** ratio. However the Kamlet−Taft′s solvatochromic parameters α and β which rates the acidity and basicity of solvents show clear differences: acidity (α) [$CHCl_3$ (0.44), CH_2Cl_2 (0.30) > acetone (0.08), THF (0.00)] and basicity (β) [CH_2Cl_2 (0.00), $CHCl_3$ (0.00) < THF (0.55), acetone (0.48)]. The more basic solvents tetrahydrofuran and acetone might shield the β-position of the polarised nitroalkene more effectively and consequently nucleophilic attack at the α-position of the nitroalkene might be favoured. Thus the difference in solvent basicity might result in a different degree of shielding of the β-position of the nitroalkene. See: [25a] M. J. Kamlet, J.-L. M. Abboud, M. H. Abraham, R. W. Taft, *J. Org. Chem.* **1983**, *48*, 2877. − [25b] Christian Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed., **1990**, VCH, Weinheim, Germany. − [25c] Freezing pressures, see for example references cited in: N. S. Isaacs, *Tetrahedron* **1991**, *47*, 8463−8497.

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